REMARKS

Claims 16-23 were pending in the application. The Examiner withdraws Claim 23 from consideration as being non-elected due to the sub-election of "the combination of all recited subtypes of Claim 1". Applicant has amended Claim 23 to correspond to the sub-election so as to have Claim 23 examined with the group to which it was originally assigned. The Claim 23 amendment does not require additional searching, since the Examiner has already conducted the search of probes to the total combination of HPV subtypes. If the amendment is not permitted, Applicants reserve the right to request that Claim 23 be rejoined, at such time as allowable claims are determined.

Claims 16-22 were rejected. Claims 16-23 have been amended. None of the amended claims introduce new subject matter. Amended claims 16 and 17 correct a typographical error which was a numerical transposition. Amended Claim 22 corrects the name of the GAPDH gene and is supported at page 46, paragraph [0098].

Objections and rejection under 35 USC § 112, second paragraph

Claims 17-22 were objected to and rejected because they referred back to Claim 1. The claims have been amended to refer to independent Claim 16, instead.

Claims 16 and 23 were amended to correspond to the election.

Claims 16 and 17 were amended to correct the numerical transposition and recite the correct species: CP8304.

Claim 22 was amended to correct a recognizable error in the spelled out name of the GAPDH gene.

It is believed these amendments to the claims, overcome all the objections and the rejection under 35 USC §112, second paragraph.

35 USC §103

Claims 16, 17, 18, 20 and 21 were rejected as being unpatentable over Bauer et al U.S. Patent No.5,527,898 in view of 1991 HPV compendium, accession number AB027021 GI:6970427; Vhow et al., *(Journal of General Virology, Vol. 80 pp. 2923-2929.(1999)); Kino et al., (Clinicall and Diagnostic Laboratory Immunology, Vol. 7. pp. 91-95. (2000))*; and Hogan et al U.S. Patent No. 5,541,308. Applicant traverses the rejection.

The Examiner indicated that Bauer teaches membrane-bound oligonucleotide probes to the L1 region of HPV, but that Bauer does not teach detection probes to HPV 6, 11, 16, 18 and 33, among others recited in the instant claims. The Examiner reasoned that it would be prima facie obvious to improve Bauer's method of HPV detection and typing to include HPV 6, HPV 11, HPV 16, HPV 18, and HPV 33, as well as the other HPV types of the invention by combining the teachings of Bauer with the teachings of the above-named references. However, this combination would not improve the Bauer method. It would, in fact be inoperable.

Bauer not only does not teach detection probes for HPV 6, HPV 11, HPV 16, HPV 18, and HPV 33, Bauer instructs that the detection probes are designed so as to avoid containing sequences that hybridize to genomic sequence from HPV types 6, 11, 16, 18, and 33 (Bauer claims 1-50). Bauer required this negative instruction, because the amplification primers Bauer teaches for amplification of HPV DNA, prior to detection, are directed to sequence from HPV types 6, 11, 16, 18 and 33 (Col. 3, lines 1-13, Col. 6 line 66 to Col. 7, line 4) and HPV types 6, 11, 16, 18 and 33 share significant homology at the DNA level, particularly at the L1 open reading frame (Col. 1 lines 37-42). Thus, the detection probes directed to these HPV types would not distinguish the HPV types. Therefore, the combination the Examiner suggested would be inoperable. The case law is clear on this issue: if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation. *In re Cordon,* 733 F.2d 90, 221 USPQ 1125 (Fed Cir. 1984). MPEP 2143.01. For this reason alone, all the claims are patentable over the prior art.

Furthermore, Bauer only discloses how to detect 15 HPVs and states that the detector cannot attach a large number of probes (Col. 10, lines 6-9). Thus, Bauer does not teach a detector which is capable of immobilizing the 39 microdots contained on the carrier of the present invention. Since the Bauer detector cannot attach a large number of probes, the Examiner's combination of Bauer with references disclosing the 39 different HPV gene sequences nevertheless does not teach or suggest how to produce the detector of the invention, since there is no combination of references showing how to make the instant detector, capable of attaching the 39 different probe oligonucleotide sequences.

Still further, the Examiner states that Bauer teaches type specific probes that are 18-20 nucleotides in length with a Tm of 58° C to 64° C, referring to Col. 9 lines 15-19. The cited paragraph of Bauer also discloses that a given probe will generally have less than 75% similarity with sequences from HPV types distinct from that recognized by the probe. This allows for a similarity of up to a little more than 74% which allows for a good deal of cross-hybridization with other HPV subtypes. Thus, even the detection probes that Bauer does teach do not meet the claim limitation of the instant invention, wherein the one oligonucleotide sequence contained in each micro-dot is specific to the one particular HPV subtype. None of the other references cited by the Examiner cure this defect. Thus the references do not render the claimed invention obvious.

Chow was cited for teaching the sequence of HTL7474-S which is the full length HPV L1AE5. However, Chow teaches that the L1 gene exhibited 78% identity to HPV types 18, 39, 45, 59, 68 and 70. Thus, again the degree of cross-hybridization is high for this HPV type to other HPV types which are recited in the limitations of the claimed invention. Thus the combination of Bauer with Chow and the other combined references does not meet the limitation of the instant invention because it does not teach an oligonucleotide sequence which is specific to the L1AE5 HPV.

Hogan was cited for teaching probe design for detection of specific sequences and detection of variable regions. However, Hogan's invention is specifically for non-viral DNA and specifically for rDNA while the DNA at issue here is viral DNA. rDNA has characteristics which distinguish it from all other types of DNA sequences, for instances, it is GC-rich. Viruses don't make rDNA. Viral DNA has characteristic which are very different from non-viral rDNA. Thus, the Examiner's rationale to use Hogan's method designed for non-viral rDNA to prepare probes for viral DNA is inoperable, unless the Examiner can provide evidence that particular teachings of Hogan are operable to drive the present invention. The Examiner has not done that. Thus, the Hogen teaching is either inoperable to the present invention or, alternatively, it teaches away from the combination that the Examiner has presented. In either case, the combination the Examiner has relied upon cannot be used to support the rejection.

Claims 19 and 22 were rejected under 35 USC § 103(a) as unpatentable over Bauer et al. (US Patent 5527898), 1997 HPV compendium, Chow et al, accession number AB027021 GI: 6970427 and Hogan et al (US Patent 5541308) as applied to claims above 16-18, 20, and 21, and further in view of Lockhart et al (US Patent 6040138).

Since claims 19 and 22 are dependent claims, and the combination of references does not teach the limitations discussed above, Claim 19 and 22 are also not obvious. In light of the above teachings of Bauer and Hogan, the Examiner's combined reference teachings including Lockhart do not provide teaching or motivation to arrive at the invention recited in any of the instant claims.

Finally, it must be emphasized that the present invention not only provides oligonucleotide probes to detect 39 different HPV subtypes, but also incorporates these probes in one membrane, wherein the respective probes have high specificity and hence will not cross-hybridize with other targets. This advancement allows the clinical diagnosis for the claimed 39 HPV subtypes to be carried out at the same time, which is more rapid and more reliable over the known schemes. The present invention satisfies the long-felt needs of the skilled person in this art, and finds a solution to the cross-hybridization of the claimed HPV subtype. Therefore, the present invention is undoubtedly nonobvious.

Based on at least the above reasons, the present application has many features never shown, taught or suggested in the citations, so that the present invention is different from the cited references; furthermore, the present invention cannot be achieved by the cited art either, since no matter what we judge from the objects, functions, elements of the architecture or method, the present invention is distinct from the cited art. Therefore, reconsideration and allowance of the present patent application are earnestly solicited at an early date.

In view of the foregoing, Applicants submit that all pending claims are in condition for allowance and request that all claims be allowed. The Examiner is invited to contact the undersigned should he believe that this would expedite prosecution of this application. It is believed that no fee is required. The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,

Dated: March 2, 2007

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